

WHAT IS CLAIMED IS:

- 1 1. A method of diagnosing PAPA syndrome in a subject comprising detecting a mutation in
2 a gene allele of the subject, wherein the gene allele encodes CD2BP1.
- 1 2. The method of claim 1, wherein the mutation is within the region of the gene that
2 encodes from amino acid 122 to 288 inclusive in CD2BP1.
- 1 3. The method of claim 1, wherein the mutation includes a G748C transversion in a
2 CD2BP1 gene.
- 1 4. The method of claim 1, wherein the mutation includes a G688A transition in a CD2BP1
2 gene.
- 1 5. The method of claim 1, wherein the detection is by denaturing HPLC.
- 1 6. The method of claim 1, wherein the detection is by DNA sequence analysis.
- 1 7. A method of diagnosing PAPA Syndrome in a subject comprising identifying a single
2 nucleotide polymorphism (SNP) in the CD2BP1 gene of the subject, comprising:
 - 1 (a) obtaining a sample of nucleic acid from the subject; and
 - 2 (b) determining the identity of one or more SNPs in the CD2BP1 gene, wherein the
3 SNPs are located at nucleotides 688 and 748 of the CD2BP1 gene.
- 1 8. The method of claim 7, wherein the determining step comprises amplifying at least a
2 portion of a nucleic acid molecule encoding the CD2BP1 gene.
- 1 9. The method of claim 7, wherein the identity of one or more SNPs is determined by DNA
2 sequence analysis.
- 1 10. A method of screening for an agent that modifies an immune response in cells that
2 express a CD2BP1 with a mutation associated with PAPA syndrome, the method comprising:
 - 3 contacting the cells with an agent suspected of modifying the immune response;
 - 4 measuring an indicator of immune response; and
 - 5 comparing the measurement to the same immune response indicator in a control cell under
6 comparable conditions in the absence of the agent;
 - 7 wherein a difference in the indicator is indicative of an agent that modifies the immune response.
- 1 11. The method of claim 10, wherein the mutation is in the region of CD2BP1 bounded by
2 amino acids 122 to 288 inclusive.

- 1 12. The method of claim 10, wherein the cells express CD2BP1 with a G668A mutation as
2 numbered in SEQ ID NO:21.
- 1 13. The method of claim 10, wherein the cells express CD2BP1 with a G748C mutation as
2 numbered in SEQ ID NO:19.
- 1 14. The method of claim 10, wherein the mutation is in amino acid 250 of the CD2BP1.
- 1 15. The method of claim 10, wherein the mutation is an E250Q mutation of the CD2BP1.
- 1 16. The method of claim 10, wherein the mutation is in amino acid 230 of the CD2BP1.
- 1 17. The method of claim 10, wherein the mutation is an A230T mutation of the CD2BP1.
- 1 18. The method of claim 10, wherein the indicator is T-cell rosetting.
- 1 19. The method of claim 10, wherein the indicator is altered motility of the cells.
- 1 20. The method of claim 10, wherein the indicator is CD2 triggered adhesion involving
2 CD58.
- 1 21. The method of claim 10, wherein the indicator is integrin-mediated adhesion activated
2 through CD2 or a CD15 carrier.
- 1 22. The method of claim 21, wherein the CD15 carrier is CD66a.
- 1 23. A method of screening for an agent that modifies an immune response in cells that
2 express a mutant CD2BP1, wherein the mutant CD2BP1 comprises a A230T mutation or a
E250Q mutation, comprising:
4 contacting the cells with an agent suspected of modifying the immune response;
5 measuring an indicator of immune response; and
6 comparing the measurement to the same immune response indicator in control cells under
7 comparable conditions in the absence of the agent;
8 wherein a difference in the indicator is indicative of an agent that modifies the immune response.
- 1 24. The method of claim 23, wherein the indicator is T-cell rosetting.
- 1 25. The method of claim 23, wherein the indicator is altered motility of the cells.
- 1 26. The method of claim 23, wherein the indicator is CD2 triggered adhesion involving
2 CD58.
- 1 27. The method of claim 23, wherein the indicator is integrin-mediated adhesion activated
2 through CD2 or a CD15 carrier.
- 1 28. The method of claim 27, wherein the CD15 carrier is CD66a.

- 1 29. A method of screening for an agent that modifies an interaction of CD2BP1 with a binding
2 partner of CD2BP1, wherein the CD2BP1 has a mutation associated with PAPA syndrome, the
3 method comprising:
- 4 measuring the binding of the CD2BP1 to a binding partner in the presence of an agent
5 suspected of altering the binding interaction of the CD2BP1 and the binding partner and
6 comparing the binding in the presence of the agent to a measured control of the binding
7 interaction in the absence of the agent, wherein a difference in the binding interaction is
8 indicative of an effector of CD2BP1 binding to a binding partner.
- 1 30. The method of claim 29, wherein the binding partner is the cytoplasmic portion of CD2,
2 PTP PEST, PTP HSCF, WASP, pyrin, c-Abl, or a CD15 carrier.
- 1 31. The method of claim 29, wherein the mutation is in the region of CD2BP1 bounded by
2 amino acids 122 to 288 inclusive.
- 3 32. The method of claim 29, wherein the mutation is in amino acid 250 of the CD2BP1.
- 4 33. The method of claim 29, wherein the mutation is an E250Q mutation of the CD2BP1.
- 5 34. The method of claim 29, wherein the mutation is in amino acid 230 of the CD2BP1.
- 6 35. The method of claim 29, wherein the mutation is an A230T mutation of the CD2BP1.
- 7 36. A method of screening for an agent that modifies an interaction of mutant CD2BP1 with
8 a binding partner of CD2BP1, wherein the mutant CD2BP1 comprises an A230T mutation or an
E250Q mutation, the method comprising:
- 1 measuring the binding of the mutant CD2BP1 to a binding partner in the presence of an
2 agent suspected of altering the binding interaction of the mutant CD2BP1 and the binding
3 partner, and comparing the binding in the presence of the agent to a measured control of the
4 binding interaction in the absence of the agent, wherein a difference in the binding interaction is
5 indicative of an effector of mutant CD2BP1 binding to a binding partner.
- 6 37. The method of claim 36, wherein the binding partner is the cytoplasmic portion of CD2,
7 PTP PEST, PTP HSCF, WASP, pyrin, c-Abl, or a CD15 carrier.
- 8 38. An isolated nucleic acid molecule or the complement thereof, wherein the molecule
1 encodes an amino acid sequence comprising the sequence of SEQ ID NO:20 or SEQ ID NO:22,
2 with conservative amino acid substitutions.
- 3 39. The molecule of claim 38, wherein the molecule encodes an amino acid sequence
4 comprising the sequence of SEQ ID NO:20.

- 1 40. The molecule of claim 38, wherein the nucleic acid molecule comprises the nucleic acid
2 sequence of SEQ ID NO:19.
- 1 41. The molecule of claim 38, wherein the molecule encodes an amino acid sequence
2 comprising the sequence of SEQ ID NO:22.
- 1 42. The molecule of claim 38, wherein the nucleic acid molecule comprises the nucleic acid
2 sequence of SEQ ID NO:21.
- 1 43. An expression construct comprising the nucleic acid molecule of claim 38 operably
2 linked to an expression control sequence.
- 1 44. The expression construct of claim 43, further defined as a plasmid expression vector or a
2 viral expression vector.
- 1 45. A host cell transformed or transfected with the expression construct of claim 43, or a
2 progeny of the cell.
- 1 46. The host cell of claim 45, further defined as a bacterial cell, a mammalian cell, or a
2 human cell.
- 1 47. An isolated nucleic acid molecule comprising about 20 contiguous nucleotides of SEQ ID
2 NO:18, including: (a) nucleotide 688 wherein the G is replaced by an A; (b) nucleotide 748
3 wherein the G is replaced by a C; or both (a) and (b).
- 1 48. The isolated nucleic acid molecule of claim 47, wherein the nucleotide corresponding to
2 nucleotide 688 of SEQ ID NO:18 is located at the 5' end of the molecule.
- 1 49. The isolated nucleic acid molecule of claim 47, wherein the nucleotide corresponding to
2 nucleotide 688 of SEQ ID NO:18 is located at the 3' end of the molecule.
- 1 50. The isolated nucleic acid molecule of claim 47, wherein the nucleotide corresponding to
2 nucleotide 748 of SEQ ID NO:18 is located at the 5' end of the molecule.
- 1 51. The isolated nucleic acid molecule of claim 47, wherein the nucleotide corresponding to
2 nucleotide 748 of SEQ ID NO:18 is located at the 3' end of the molecule.
- 1 52. An isolated nucleic acid molecule comprising the complement of the nucleic acid
2 molecule of claim 47.
- 1 53. An array of nucleic acid molecules attached to a solid support, the array comprising an
2 oligonucleotide that will hybridize to the nucleic acid molecule of claim 47, under conditions in
3 which the oligonucleotide will not substantially hybridize to a nucleic acid molecule consisting
4 of SEQ ID NO:18.